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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,046	12/15/2000	Philip L. Felgner	GTSYS.004A	2320
20995	7590	05/06/2004	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			LUCAS, ZACHARIAH	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/738,046

Applicant(s)

FELGNER ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 1-13, 20, 24 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-19, 21, 22, 23, 26, and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 4 lists.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Claims 14-19, 21-23, 26, and 27 are under consideration. Claims 1-13, 20, 24, and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the paper filed February 27, 2004.
2. Applicant's election of Group II, and subgroups (B) and (i) the paper filed February 27, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
3. It is further noted that the Applicant referred to the elects of the subgroups as species elections. This is incorrect. The subgroups identify distinct inventions falling within the indicated groups.

### ***Information Disclosure Statement***

4. The information disclosure statements (IDS) submitted on April 19, 2001, June 18, 2001, October 10, 2003, and March 1, 2004, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.
5. It is noted that reference 2 on the October 10, 2003 IDS and reference 4 on the June 2001 IDS have been crossed off in the lists of references cited by the Applicant. This is because the indicated references are international search reports on related PCT applications. These search reports cite the other references listed in the information disclosure statements, but are not

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themselves references. Thus, the search reports have been crossed out as they have not been considered separately from the documents cited therein (and in the respective IDS).

6. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

WO 99/08997 (reference 3 in the June 2001 IDS).

### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim describes the method of claim 14, wherein the delivery composition “is the composition of claim 1.” Claim 1 describes a delivery composition comprising “a protein in operative association with a cationic intracellular delivery vehicle... wherein the intracellular delivery vehicle is adapted to fuse with a cell-membrane.” It is unclear what is meant by the phrase requiring an “operative association” between the protein and the vehicle. It is further unclear how the delivery vehicle is “adapted to fuse with a cell membrane.” While the Applicant describes the making of delivery vehicles that appear capable of such fusion, it is not clear what adaptation is being performed.

### ***Claim Rejections - 35 USC § 102***

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9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 14, 15, 26, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Walker et al.(PNAS 89:7915-18- of record in the October 2003 IDS). The claims read on methods for the delivery of a protein into a cell by contacting the cell with a protein associated with a cationic lipid. The reference teaches the use of a cationic lipid associated with an immunogenic protein such that the protein was delivered into a cell. The reference therefore anticipates the indicated claims.

11. Claims 14, 15, 19, 22, 26, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by either of U.S. Patent 5,459,127 or Zhou et al. (J Drug Target 3(2): 91-109). The claims read on methods for the delivery of a protein into a cell by contacting the cell with a protein associated with a cationic lipid. The patent teaches the use of cationic lipid containing particles for the intracellular delivery of proteins. See e.g., claims 1, 2, 30, 33, 34, 42, and columns 6-7 (teaching that the claimed compositions of the patent include cationic lipids and proteins, or polynucleotides encoding proteins, which may be therapeutic peptides or immunogens). Zhou teaches that cationic liposomes are used for the delivery of negatively charges antigenic peptides

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into MHC cells for processing into immune response pathways. See .g., pages 95-96. The references therefore anticipate the indicated claims.

12. Claims 14, 15, 19, 22 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,348,499. The claims read on methods for the delivery of a protein into a cell by contacting the cell with a protein associated with a cationic lipid. The 499 patent teaches the use of a disclosed set of cationic lipids for the delivery of polypeptides into cells. Columns 4-5. The reference teaches that this can be achieved by the fusion of liposomes comprising the lipids with the cell membrane, thereby resulting in the intracellular delivery. Id. The reference therefore anticipates the indicated claims.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

13. Claims 14-19, and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,165,720. These claims read on methods of delivering a protein into a cell wherein the protein is conjugated to a nucleic acid, and wherein the conjugation is through a peptide nucleic acid (PNA) linker. The 720 patent teaches the conjugation of a peptide or protein with a PNA, and through the PNA to a nucleic acid, and that such proteins or peptide may be

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immunostimulatory peptides. See e.g., column 3, lines 40-45; and col. 8, lines 59-62. The reference also teaches the delivery of such conjugates into cells using cationic lipid mediated transfection. Col. 10, lines 25-41. Thus, the reference teaches the conjugation of therapeutic (immunostimulatory) proteins to nucleic acids through PNA linkers, and the transfection of such conjugates into cells. The reference therefore anticipates the indicated claims.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

### ***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 14, 15, 19, 21-23, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of either of Hughes et al. (U.S. Patent 6,169,078) in view of Dzau et al. (U.S. Patent 5,631,237). The claims have been described above.

Hughes teaches that cationic lipid compositions may be used for the delivery of proteins (and other compositions) into cells. See, claims 1 and 2; and column 4, lines 15-37. The

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reference also teaches that such delivery may be made by way of either a complex between the protein and the lipid, or a liposome containing the agent. Col. 4, lines 51-62. Thus, the reference renders obvious the association of cationic lipids with proteins for the delivery of the proteins into cells. Hughes teaches that the cationic lipids may be used for the delivery of proteins generally, thus, the reference would have provided both suggestion and an expectation of success for the use of cationic lipids to deliver proteins in general into cells. Dzau teaches that proteins that those in the art may wish to deliver into cells include therapeutic peptides, and proteins that act as inhibitors, including antibodies. Column and col. 12, lines 37-49. It would therefore have been obvious to those in the art to deliver any of the types of proteins indicated in claims 21-23, 26, or 27 into cells by associating them with cationic lipids as described in Hughes, and contacting the cells with the resulting compositions.

### ***Double Patenting***

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 14, 15, 19, 22, 26, and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-44 of U.S. Patent No.

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5,459,127. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of the patent claims are species of the genus of inventions described in the claims of the present application.

18. Claims 14-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/705365 (now allowed). Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are generic to the allowed species claims of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 14-19, 22, 26, and 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15, 16, and 20-24 of copending Application No. 10/141535 in view of the teachings of Zhou (supra). The claims of the present application have been described above. The claims of the copending application describe a method of delivering a polypeptide through use of an intracellular delivery vehicle into an APC cell. The claims of the present application encompass the species of the copending application. However, neither the present claims, nor those portions of the specification describing the claimed invention teach the species claimed in the copending application.

However, the Zhou reference teaches the administration of antigenic polypeptides through cationic delivery vehicles into APCs for processing in immune response systems. See

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.g., pages 95-96. Further, this reference teaches that the cationic liposomes are limited to the delivery of negatively charged antigens. The current application teaches that, in certain embodiments of the claimed invention, the protein is bound to a negatively charged polymer, which in turn could bind to the cationic lipids of a delivery vehicle. App. pages 6-7. In view of these teachings, and the prior art teachings of Zhou, it would have been obvious to those in the art that the claimed invention of the present application could be used for the delivery of either positively or negatively charged antigens (through the association with the negatively charged oligonucleotide polymers) into APC cells. Thus, the claims of the copending application are an obvious variation to the presently claimed invention.

This is a provisional obviousness-type double patenting rejection.

### ***Conclusion***

20. No claims are allowed.

21. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

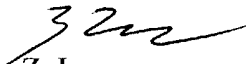
Lutziak et al., J Pharm Sci, 87(11): 1428-32. This reference teaches the use of liposomes into APCs. The reference is considered redundant to the teachings of Zhou.

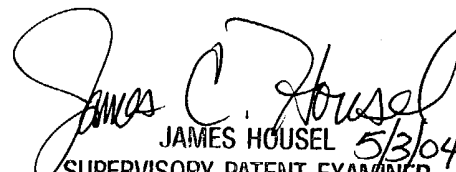
22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Z. Lucas  
Patent Examiner

  
JAMES HOUSEL 5/3/04  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600